

## **REMARKS**

In accordance with the foregoing, claims 15 and 17-19 are amended. New claims 26-32 are added. Claims 15, 17-19, and 26-32 are pending and under consideration.

No new features and/or new matter have been added and accordingly, entry and approval of claims 15, 17-19, and 26-32 is respectfully requested.

### **I. AMENDMENT TO THE CLAIMS**

Independent claim 15 has been amended to set forth a method for preserving food comprising bringing food into contact with sintered Ti-modified calcium hydroxyapatite for storage. The Ti-modified calcium hydroxyapatite has a part of calcium in calcium hydroxyapatite substituted with titanium. The Ti-modified calcium hydroxyapatite is sintered from 580 to 660°C so that photocatalytic activity of the Ti-modified calcium hydroxyapatite may be enhanced. The food is brought into contact with the sintered Ti-modified calcium hydroxyapatite by putting the food in a container having an inner surface coated with the sintered Ti-modified calcium hydroxyapatite or in a container made of a material containing the sintered Ti-modified calcium hydroxyapatite.

Claim 15 has been amended only to clarify that the preparing and sintering of the Ti-modified calcium hydroxyapatite are not performed at the time of preserving the food. No change in the scope or meaning of the claim is intended. Similar amendments have been also made to independent claims 17-19.

### **II. REJECTION OF THE CLAIMS UNDER 35 U.S.C. § 103**

The instant Office Action rejects claims 15 and 17-19 under 35 U.S.C. § 103 over various combinations of:

1. U.S. Patent 5,658,530 to Dunn (hereinafter "Dunn")
2. JP2000-327315 to Wakamura et al. ("Wakamura"),
3. U.S. Patent No. 5,614,568 to Mawatari et al. ("Matawari"),
4. U.S. Patent No. 4,367,312 to Bontinck et al. ("Bontinck"),
5. U.S. Patent No. 6,004,667 to Sakurada et al. ("Sakurada1"),

6. JP11343210 to Sakurada ("Sakurada2")
7. JP03275627 to Saito ("Saito"),
8. JP2000-095577 to Hirade et al. ("Hirade"),
9. U.S. Patent No. 5,468,489 to Sakuma et al. ("Sakuma"),
10. JP04170960 to Atsumi et al. ("Atsumi1"), and
11. JP04217902 to Atsumi ("Atsumi2").

In the instant Office Action, the Examiner incorporates many of the arguments from the Office Action of February 5, 2009 (hereinafter "previous Office Action"). Dunn serves as the primary reference in paragraphs 4 and 5 of the instant Office Action and paragraphs 8 and 9 of the previous Office Action. Wakamura serves as the primary reference in paragraphs 6-8 of the instant Office Action and 12-14 of the previous Office Action.

**i. Unexpected Results of Sintering Ti-modified Calcium Hydroxyapatite Sintered from 580 to 660°C.**

As Applicant has repeatedly pointed out, the claimed method has arisen from a finding that the antibacterial effect of Ti-modified calcium hydroxyapatite (hereinafter "Ti-CaHAP"<sup>1</sup>) is unexpectedly enhanced by preliminary sintering at 580 to 660°C in comparison with non-sintered or otherwise sintered Ti-modified calcium hydroxyapatite. A comparison of Example 3 (sintered) to Example 1 (non-sintered) and Example 4 (sintered) to Example 2 (non-sintered) in the Specification provides experimental support for this unexpected enhancement. From Fig. 3 of the Specification,<sup>2</sup> note that sintered Ti-CaHAP provides a higher antibacterial effect than non-sintered Ti-CaHAP, in spite of the fact that Ti-CaHAP is otherwise the same in Examples 1-4.

**ii. The References, Alone or in Combination, Neither Disclose nor Suggest a Ti-CaHAP Wherein a Part of the Calcium has been Substituted with Titanium and that has been Sintered Between 580 to 660°C for Enhancing Photocatalytic Activity.**

The Examiner asserts that it would have been obvious to sinter a Ti-modified CaHAP at 580 to 660° C for enhancing photocatalytic activity.

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<sup>1</sup> See page 11, lines 20-22 for an example usage of this abbreviation.

<sup>2</sup> In Fig. 3, A3 and A1 represents the storage under light exposure of sintered and non-sintered Ti-CaHAP, respectively. A4 and A2 represents the storage without light exposure of sintered and non-sintered Ti-CaHAP, respectively.

While Dunn (US Patent No. 5,658,530) may disclose a titanium dioxide ( $\text{TiO}_2$ ) as a catalyst, Dunn fails to teach or suggest Ti-modified calcium hydroxyapatite. In the February 5, 2009 Office Action, the Examiner admits that Dunn fails to disclose the use of Ti complexed with calcium hydroxyapatite on page 6.

Wakamura (JP 2000-327315) may disclose Ti-modified calcium hydroxyapatite, but Ti-CaHAP is heated only to  $100^\circ\text{C}$  (see Paragraphs [0019] and [0021]), which is far less than the claimed temperature range of  $580$  to  $660^\circ\text{C}$ . Further, Wakamura fails to teach or suggest the use of Ti-CaHAP for food preservation.

Mawatari fails to teach or suggest **Ti-modified** calcium hydroxyapatite. Mawatari merely teaches calcium hydroxyapatite as an example of a support for a metal catalyst such as silver (column 7, lines 25-49), Mawatari neither discloses nor suggests a Ti-CaHAP wherein a part of calcium in calcium hydroxyapatite is substituted with titanium. Further, while Mawatari may describe sintering or calcination, such sintering or calcination is performed at  $800^\circ\text{C}$  or higher and only to strengthen a bonding of silver on a calcium hydroxyapatite support (column 7, lines 43-9). Mawatari does not perform sintering or calcination to enhance photocatalytic activity of Ti-CaHAP.

Further, the Examiner admits that the combination of Dunn and Wakamura are silent with regard to sintering Ti-modified calcium hydroxyapatite at  $580$  to  $600^\circ\text{C}$  on page 3.

Similarly, Bontinck (US Patent No. 4,367,312) fails to teach or suggest a Ti-CaHAP wherein a part of calcium in calcium hydroxyapatite is substituted with titanium. Bontinck also does not teach or suggest sintering Ti-CaHAP at  $580$  to  $660^\circ\text{C}$  to enhance photocatalytic activity of a Ti-modified calcium hydroxyapatite. The Examiner admits that Bontinck is unrelated to Ti-CaHAP in paragraph 13.

Sakurada1 (US Patent No. 6,004,667) merely describes combining a photocatalytic film made of, for example,  $\text{TiO}_2$  with an adsorbent such as hydroxyapatite (column 6, lines 49-63). Thus, Sakurada1 fails to teach or suggest a Ti-CaHAP wherein a part of calcium in calcium hydroxyapatite is substituted with titanium. Nor does Sakurada1 teach or suggest sintering such a Ti-CaHAP at  $580$  to  $660^\circ\text{C}$  for enhancing photocatalytic activity of the Ti-CaHAP.

Sakurada2 (JP 11-343210) merely teaches a combination of photocatalytic powder (e.g.  $\text{TiO}_2$ ), metal powder (e.g. gold, silver) and an adsorbent material such as hydroxyapatite (Abstract). Thus, Sakurada2 fails to teach or suggest a Ti-CaHAP wherein a part of calcium in calcium hydroxyapatite is substituted with titanium. Nor does Sakurada2 teach or suggest

sintering such a Ti-CaHAP at 580 to 660°C for enhancing photocatalytic activity of the Ti-CaHAP.

The Examiner asserts that “Saito (JP 03-275627) teaches replacing the metal ion on apatite with an antimicrobial metal” and sintering at 600°C. Saito describes sintering at a temperature of no less than 300° C. However, Saito only enumerates Ag, Cu, Zn, Sn, Hg, Pb and Cd as examples of acceptable antimicrobial metals, not titanium. Of those antimicrobial metals, Saito actually tests only Ag and Cu in the working examples (see Examples and Table 1). Saito does not mention titanium. Further, Saito describes sintering at a temperature of no less than 300°C to firmly fix the metal ion, not to enhance photocatalytic activity. Thus, Saito, also fails to teach or suggest Ti-CaHAP wherein a part of calcium in calcium hydroxyapatite is substituted with titanium. Nor does Saito teach or suggest sintering such a Ti-CaHAP at 580 to 660°C for enhancing photocatalytic activity of the Ti-CaHAP.

**The Examiner’s sole argument as to why one would have been motivated to combine the references with Dunn and Wakamura is that “Saito teaches that heating of a metal modified calcium hydroxyapatite results in improved fixing of the metal onto the hydroxyapatite thus preventing the metal from dissolving out.”**

In response, Applicant wishes to emphasize again that Saito only discloses apatite partially replaced with Ag, Cu, Zn, Sn, Hg, Pb or Cd (of which only Cu and Ag were tested), not Ti-CaHAP. Saito never teaches that the photocatalytic activity of Ti-CaHAP is enhanced by preliminary sintering at a temperature range of 580 to 660°C. Titanium is a different metal from those described in Saito, occupying a position in the periodic table at least 7 groups to the left of any of the Saito metals. Titanium has a significantly different melting temperature, and different chemical properties from the Saito metals. If this rejection is maintained in the next Office Action, Applicant respectfully requests that the Examiner state how it would have been obvious to one of ordinary skill in the art that the sintering temperatures of Saito would be applicable to Ti-CaHAP and how it would have been obvious that sintering would result in enhancing photocatalytic activity of Ti-CaHAP as claimed.

Without such explanations, it appears that Dunn, Wakamura, and Saito have been combined based on the knowledge of the unexpected advantages that may result from the claimed sintering of Ti-CaHAP, information provided by the Application. There is impermissible hindsight when an “‘express’ motivation to combine the references is lacking.” See MPEP 2145. An applicant may rebut the obviousness of a combination of

**two or more references by demonstrating “the claimed invention yields unexpectedly improved properties or properties not present in the prior art.” MPEP 2145. Therefore, the Examiner must substantiate his position that it would have been obvious to one having ordinary skill in the art to combine Dunn, Wakamura, and Saito to enhance photocatalytic activity of Ti-CaHAP by preliminary sintering at a temperature range of 580 to 660°C.**

Hirade (JP2000-095577) teaches a mere composite of hydroxyapatite (element 4a in Figure 2) with titanium (element 4b inside element 4a). Hirade, like the references discussed above, also fails to teach or suggest Ti-CaHAP wherein a part of calcium in calcium hydroxyapatite is substituted with titanium, let alone sintering Ti-CaHAP at 580 to 660°C for enhancing photocatalytic activity of the Ti-CaHAP.

Further, while the Examiner asserts that Hirade teaches sintering a titanium calcium hydroxyapatite at up to 600° C, the Examiner admits that it is unclear whether “Hirade teaches that the calcium hydroxyapatite is modified by the titanium metal.” Previous Office Action at page 9-10. Applicant notes that titanium and hydroxyapatite are referred to collectively as a “composite” throughout the Hirade reference.

“A rationale to support a conclusion that a claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art.” MPEP 2143.02. “In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required.” MPEP 2164.03.

Hirade cannot be used to reject the claims. The Examiner is essentially arguing that the effect of sintering a Ti-CaHAP in a specific temperature range can be predicted from teachings directed to an unknown or different chemical relationship between two compounds. Such an analysis is impermissible in a rejection based on 35 U.S.C. § 103.

Shimazaki (JP63-023744) may describe a mixture of hydroxyapatite (partially substituted with an alkali metal or alkali earth metal) and an oxide or composite oxide of an element selected from Mg, Sr, Ba, B, Si, P, Ti, Zr, Nb, Mo, Ta, W, Bi and Co (Abstract). However, like the references discussed above, Shimazaki also fails to teach or suggest Ti-CaHAP wherein a part of calcium in calcium hydroxyapatite is substituted with titanium, let alone sintering Ti-CaHAP at 580 to 660°C to enhance photocatalytic activity of the Ti-CaHAP.

Sakuma (US5468489) may describe a dentifrice (tooth paste or powder) that comprises combining an antibacterial metal with a calcium hydroxyapatite so that the calcium hydroxyapatite may serve as a carrier for the antibacterial metal. However, Sakuma only enumerates Ag, Zn and Cu as examples of antibacterial metals. Further, Sakuma adopts a sintering temperature of no less than 800°C (column 2, lines 25-49) which is far higher than the claimed range, as already noted by the Examiner. Sakuma also fails to teach or suggest Ti-CaHAP wherein a part of calcium in calcium hydroxyapatite is substituted with titanium, let alone sintering of Ti-CaHAP at 580 to 660°C for enhancing photocatalytic activity of the Ti-CaHAP.

Atsumi1 (JP04-170960) merely describes combining Ag and Zn with calcium hydroxyapatite, and sintering at a temperature of at least 800°C (English abstract). Thus, Atsumi et al also fails to teach or suggest Ti-CaHAP wherein a part of calcium in calcium hydroxyapatite is substituted with titanium, let alone sintering Ti-CaHAP at 580 to 660°C to enhance photocatalytic activity of the Ti-CaHAP.

Similarly, Atsumi2 (JP04-2170902) merely describes combining Ag, Cu, Zn and Ni with calcium hydroxyapatite, and sintering at a temperature of at least 800°C (English abstract). Thus, Atsumi2 (JP04-2170902) also fails to teach or suggest Ti-CaHAP wherein a part of calcium in calcium hydroxyapatite is substituted with titanium, let alone sintering Ti-CaHAP at 580 to 660°C to enhance photocatalytic activity of the Ti-CaHAP.

Okamoto (JP 2000-051041) merely teaches titanium dioxide (TiO<sub>2</sub>) as a catalyst but fails to teach or suggest Ti-CaHAP wherein a part of calcium in calcium hydroxyapatite is substituted with titanium, let alone sintering Ti-CaHAP at 580 to 660°C to enhance photocatalytic activity of the Ti-CaHAP.

**iii. The Cited References do not Show that it Was Conventional in the Art to Sinter a Ti-modified CaHAP at the Claimed Temperature Range.**

The Examiner asserts that “the art taken as a whole provides motivation for heating within applicants’ claimed range, for the purpose of improving the stability of the metal modified hydroxyapatite.” In the previous Office Action, the Examiner further asserts that

The art taken as a whole also teaches metals which have antimicrobial activity which can be sintered at a variety of temperatures such as 500°C, 600°C and 800°C, for the similar purpose of improving the antibacterial/antimicrobial activity of the metal modified calcium hydroxyapatite...[and] improved bonding, the art taken as a whole fairly teaches that [the claimed sintering temperature range for Ti-CaHAP] would have been an obvious result effective variable routinely determinable by experimentation.

On the contrary, the references cited by the Examiner overwhelmingly teach away from the claimed temperature range. Sakuma may disclose antibacterial calcium hydrogenphosphate, but again, the composition using Ag, Zn or Cu is heated at **no lower than 800°C**. The compositions of Atsumi1 (JP04-170960) are preferably sintered at temperatures of **at least 800°C** because 800°C is the point wherein crystal growth proceeds rapidly, allowing bonds between silver or zinc and hydroxyapatite to be strengthened (see page 7). Atsumi1 further teaches that temperatures of **at least 961 °C** are especially preferable (English Abstract). "When the antibacterial hydroxyapatite obtained by causing it to adsorb and support a silver salt... is fired at a temperature that is not lower than 961 °C, **which is the melting point of silver, the mutual bonding of the silver, zinc, or their ions and the hydroxyapate is further strengthened.**" Atsumi1 at page 7. Similarly, Mawatari teaches that antibacterial ceramics "are calcined at high temperatures, preferably at **800°C or higher**" so that "the **bonding of the silver** supported thereon to the ceramics is strengthened, and the ceramics per se are shrunk and stabilized by calcination, so that the silver supported is not dissolved out by water-treatment." It should be noted that the Examiner admits that 800°C is above the claimed temperature range, yet bases his motivation to combine the references on the benefits of sintering above 800° C.

While Sakuma, Atsumi1, Atsumi2, and Mawatari may provide a motivation for high temperature sintering, the motivation is to sinter **above 800°C**. Atsumi1 is essentially teaching that temperature selection should be based in part upon the melting point of the metal to be added (e.g. Atsumi1). **If one of ordinary skill in the art were to apply the principle of Atsumi1 to a Ti-modified CaHAP, then one would use a sintering temperature based on the melting point of titanium (1,649°C). Clearly 1,649°C is much greater than the claim temperature range.**

Further, as discussed above, each reference that the Examiner cites for sintering at the claimed temperature range does not relate to a Ti-modified CaHAP. In fact, these references appear to be collectively teaching away from sintering titanium.

Between Saito, Sakuma, both Atsumi references, and Mawatari, only the elements of Ag, Cu, Zn, Sn, Hg, Pb, Cd, and Ni are enumerated. A closer look at these elements show that they occupy a clearly defined region on the periodic table, the nearest member being seven groups away from titanium.

It is difficult to see how the temperature ranges of these references can be used to disclose anything about sintering a Ti-CaHAP. Saito, Sakuma, the Atsumi references, and

Mawatari account for five of the six sources used by the Examiner to argue that it would have been conventional to sinter a Ti-modified CaHAP at the time of the invention. Yet the elements to which these temperature teachings are directed are far away from the titanium on the periodic table. It is common knowledge in the art that chemical properties change as one goes from left to right on the periodic table, and that elements with the most similar properties are arranged in the same groups. Therefore, it would not have been obvious from any of these references to sinter a Ti-CaHAP at the claimed range for enhancing photocatalytic activity of the Ti-CaHAP.

Aside from these five references, the Examiner only relies on Hirade to assert that it would have been obvious to sinter a Ti-CaHAP at the claimed temperature range. However, as discussed above, the Examiner admits that the nature of the composition disclosed by Hirade is unclear.

**iv. Saito and Hirade Cannot be Combined with Mawatari, Sakuma, or Either Atsumi Reference.**

As argued above, Mawatari, Sakuma, and both Atsumi references specifically teach sintering at or above 800° C while Hirade may teach sintering at or below 600° C and Saito teaches sintering above 300° C, but highest temperature practiced is 600° C.

These two groups of references are cited to disclose sintering at the claimed temperature range, but they contain opposite teachings regarding which temperatures should be used. Therefore, the references cannot be combined.

**v. Claims 15 and 17-19 are Patentable Over the References Cited**

In accordance with the foregoing arguments, it is clear that claims 15 and 17-19 are patentably distinguishable over the references cited at least with respect to:

- preparing Ti-modified calcium hydroxyapatite in which a part of calcium in calcium hydroxyapatite is substituted with titanium;
- sintering the Ti-modified calcium hydroxyapatite at 580 - 660°C for enhancing photocatalytic activity of the Ti-modified calcium hydroxyapatite.

Therefore, a prima facie case of obviousness has not been made. Even if a prima facie case of obvious has been made, the methods of claims 15 and 17-19 present unexpected advantages and are therefore nonobvious over the references cited. Therefore, the rejection to claims 15 and 17-19 should be withdrawn, which is respectfully requested.



### III. THE NEW DEPENDENT CLAIMS 26-32

To further distinguish over the combination of references, new dependent claims 26-28 have been added. Each of new claims 26-28 recite:

wherein the inner surface of the container is coated with a sol-gel solution containing a silica alkoxide and a powder of the sintered Ti-modified calcium hydroxyapatite

Antecedent basis may be found on page 15, lines 25 to page 16, line 4 of the Specification.

Regarding new dependent claims 29-32, antecedent basis may be found on page 19, lines 5-8 of the Specification. The limitation recited in each of new claims 29-32 is intended to emphasize the unexpected advantage of the claimed method over known TiO<sub>2</sub>. While TiO<sub>2</sub> has little or no photocatalytic activity in the absence of ultraviolet irradiation, the claimed Ti-CaHAP may also be effective when the food is preserved without ultraviolet irradiation (though Ti-modified calcium hydroxyapatite and TiO<sub>2</sub> are similarly effective with ultraviolet irradiation). Support for this unexpected advantage may be found in Examples 1-4 and Comparative Examples 1 and 2 of the Specification, the results of which are shown in Figs. 3 and 4. These examples also show a second unexpected advantage that may be achieved by the claimed method. The antibacterial effect of the Ti-CaHAP without ultraviolet irradiation may be enhanced by sintering at 580 to 660°C in comparison with non-sintered or otherwise sintered Ti-modified calcium hydroxyapatite (see line A4 in comparison with line A2 in Fig. 3).

Applicant notes that the TiO<sub>2</sub> of Dunn, or TiO<sub>2</sub> in general, has little or no photocatalytic activity in the absence of ultraviolet irradiation. However, because of the nonobviousness of the advantages described above, no skilled artisan would have been motivated to replace TiO<sub>2</sub> with the claimed Ti-CaHAP of the present invention.

### IV. CONCLUSION

There being no further outstanding objections or rejections, it is submitted that the application is in condition for allowance. An early action to that effect is courteously solicited.

Finally, if there are any formal matters remaining after this response, the Examiner is requested to telephone the undersigned to attend to these matters.

If there are any additional fees associated with filing of this Amendment, please charge the same to our Deposit Account No. 19-3935.

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Respectfully submitted,

STAAS & HALSEY LLP

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By: John E. Hillert  
John E. Hillert  
Registration No. 64,296

1201 New York Avenue, N.W., 7th Floor  
Washington, D.C. 20005  
Telephone: (202) 434-1500  
Facsimile: (202) 434-1501